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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
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ART UNIT	PAPER NUMBER
1633	

NOTIFICATION DATE	DELIVERY MODE
04/17/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/530,712	ELOIT ET AL.	
	Examiner	Art Unit	
	MICHAEL BURKHART	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12/29/2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *22-60* is/are pending in the application.

4a) Of the above claim(s) *25,30,36-51 and 56-60* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *22-24,26-29, 31-35 and 52-55* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of Group I, and the species of "type 2 canine adenovirus" and "cat", in the reply filed on 12/29/2008 is acknowledged.

Claims 25, 30, 36-51, and 56-60 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected inventions and species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 12/29/2008.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 22-24, 26-29, 31-35 and 52-55 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 22 recites the limitation "the genome of a corresponding unmodified replicating adenovirus" in lines 2-3. There is insufficient antecedent basis for this limitation in the claim. This rejection affects all dependent claims. The lack of antecedent basis for this phrase renders the claim confusing as to what is deleted: a portion of the recombinant adenovirus genome, or a part of the corresponding unmodified adenovirus genome. The metes and bounds of the claim are further confused by the fact that many "unmodified" adenoviruses do not comprise twelve encapsidation signals as recited in claim 22, and do not comprise a sequence that corresponds to

positions 311-319 of SEQ ID NO: 12 (see 35 USC 102 rejection below). It would be remedial to limit claim 22 to a canine type 2 adenovirus that comprises a deletion of residues 311-319 of SEQ ID NO: 12.

Claim 26 recites that the recombinant adenovirus of claim 22 comprises a deletion of all or a part of a region located between positions 311 to 319 of SEQ ID NO: 12. This limitation is already found in claim 22, and therefore is redundant and confusing as to what regions must be deleted to meet the claim limitations.

Claim 55, drawn to a plasmid, is dependent upon the method claim 57, which does not provide antecedent basis for the term "the nucleic acid molecule" found in claim 55. This was pointed out in the restriction requirement but has not been corrected. Claim 55 has been treated as dependent upon claim 52 in order to further prosecution.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 32-35 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. **This is a new rejection necessitated by amendment of the claims (claims 32-35 are new, and do not correspond to any previously examined claims).**

The test of enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the application coupled with information known in the art without undue experimentation (*United States v. Telectronics,* Inc. 8 USPQD2d 1217 (Fed. Cir. 1988)). Whether undue experimentation is required is a conclusion reached by weighing several factors. These factors were outlined in *Ex parte Forman*, 230 USPQ 546 (Bd. Pat. App. & Inter. 1986) and again in *In re Wands*, 8 USPQQ2d 1400 (Fed. Cir. 1988) and include the following:

Unpredictability of the art and State of the art. The art concerning the treatment of any given subject (which by implication has a given disease) by administration of an adenovirus comprising a relatively small deletion in the packaging domain is unpredictable. Adenoviruses in general are not known to cure disease, but rather, are, in general, relatively benign pathogens of the species they infect, causing a variety of symptoms (see the review by Graham et al, 2007, provided by applicants in the response dated 8/29/2007). Generally, attenuated adenoviruses may be used as vaccines against themselves (page 5, first ¶ of Graham et al). The examples in the instant specification underscore this, as an adenovirus essentially as set forth in claim 22 (CAV 311-319 control from Example 4) did not induce any immune response to a heterologous antigen (i.e. GFP in this case). Thus, the state of the art regarding the treatment of any given subject using an attenuated adenovirus as set forth in claim 22 is poorly developed. The development of such methods and adenoviruses would have to be done empirically as they are not found in the prior art, nor are they disclosed in the specification.

Number of working examples and Amount of guidance. Applicants have provided no working examples of treating a given subject, even the elected species of cat, with an attenuated adenovirus as recited in claim 22. What is disclosed (e.g. Example 4) is the expression of a

heterologous gene by the attenuated adenoviruses, wherein such expression may induce antibodies specific to the heterologous gene product. This is, however, a much more narrow scope than the instant claims, which do not recite a heterologous gene and are not limited to methods of inducing antibodies (e.g. claim 33 recites treating any type of cancer). Applicants provide no direction or guidance for the claimed methods, which require treatment of literally any disease, in literally any subject (including human) using merely an attenuated adenovirus. The specification requires the skilled artisan to practice trial and error experimentation with various and sundry attenuated adenoviruses to determine which (if any) will be efficacious as claimed.

Scope of the invention and Nature of the invention. The claims are broad in nature and read on treating any given disease, from Alzheimer's to AIDS, by merely administering an adenovirus with, as can best be determined, a small ~8 base pair deletion in the packaging domain. The invention involves the unpredictable art of treating any given subject (which by implication has a given disease) by administration of an adenovirus comprising a relatively small deletion in the packaging domain.

Level of skill in the art. While the level of skill in the art of manipulating adenoviruses, and using adenoviruses to induce antibodies to heterologous proteins, is high, the level of skill in the art of using attenuated adenoviruses to treat a broad genus of diseases is low. The unpredictability of the art, lack of guidance, broad scope of the claims and poorly developed state of the art would require that undue and excessive experimentation would have to be conducted by the skilled artisan in order to practice the claimed invention.

Given the above analysis of the factors which the courts have determined are critical in determining whether a claimed invention is enabled, it must be considered that undue and excessive experimentation would have to be conducted by the skilled artisan in order to practice the claimed invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 22, 23, 26-28, 31, 32, 34, 35 and 52-55 are rejected under 35 U.S.C. 102(b) as being anticipated by Eloit et al (J. Gen. Virol., 1995, of record) as evidence. **This is a new rejection necessitated by amendment of the claims.**

Claim 22, from which all other claims depend, is a new claim, and most closely resembles canceled claim 2. Significantly, the claims have been amended from a product-by-process format to their instant incarnation, which are unclear for reason set forth above. Whereas previous claim 1 recited an adenovirus obtained by deleting a portion of its genome, the instant claims make a comparison between the claimed recombinant adenovirus and a corresponding unmodified adenovirus. There is no way to assess with certainty what is to be deleted in the claimed recombinant adenovirus, partly for the antecedent basis issue set forth above, and for the following reasons. First, the claims are not limited to any particular

recombinant adenovirus or a particular "unmodified replicating adenovirus." Many adenoviruses do not comprise twelve encapsidation signals in the packaging domain as recited in claim 22 (e.g. adenovirus type 5 only comprises seven, see below). Thus, it is unclear how this can be a basis for what is to be deleted from the claimed recombinant adenovirus: if adenovirus type 5 (Ad5) is taken as the "corresponding unmodified adenovirus" how can a region that does not exist in the unmodified adenovirus be deleted? The specification provides no help regarding this limitation with the exception of canine type 2 adenoviruses, which have the recited twelve encapsidation signals. Thus, with respect to adenoviruses having less than twelve encapsidation signals, this limitation has been interpreted to mean that none of the encapsidation signals are deleted, e.g. for human Ad5, all seven of the known encapsidation signals must be present.

Furthermore, with respect to human Ad5, there is no sequence that "corresponds to a deletion in the segment between positions 311-319 in SEQ ID NO: 12" because there is no sequence in human Ad5 that corresponds to SEQ ID NO: 12 in general, but, more importantly, there is no such sequence that corresponds to positions 311-319 of SEQ ID NO: 12 specifically. A search of the USPTO patent nucleic acid databases and public nucleic acid databases (i.e. GenBank) revealed no homology between SEQ ID NO: 12 and any human adenovirus sequence, and an attempt to align positions 1-360 of SEQ ID NO: 12 with the human Ad5 genomic sequence (even using parameters for somewhat similar sequences) revealed no significant homology other than short (i.e. 12-15 base pair) segments, none of which included positions 311 - 319 of SEQ ID NO: 12. This attempted alignment is provided in order to complete the record. Thus, because human Ad5 does not comprise any sequence that corresponds to positions 311-

319, it is considered to inherently have a deletion of such positions relative to viruses that do comprise SEQ ID NO: 12 (i.e. canine adenovirus type 2).

Eloit et al teach a human Ad5-based recombinant virus termed Ad-gD-E1A, that replicates, at least, in human 293 cells and comprised an intact E1 gene (see the abstract, Fig. 1, Fig. 2 and the ¶ linking pages 1584-1584). This virus comprised the human Ad5 encapsidation signals I-V in their natural positions (see Fig. 1, "AI", etc.), and, essentially, nucleotides 1-455 of the Ad5 genome (page 1584, second column, first full ¶, the description of pMLP-gD). This region of Ad5 inherently has all seven of the known encapsidation signals of human Ad5 according to Schmid et al, all of which are found between nucleotides 194-380 (see the abstract and Fig. 1 of Schmid et al). Ad-gD-E1A comprised a heterologous sequence (gD) from the pseudorabies virus (abstract, Fig. 1), and comprised the E2 and E4 genes, absent evidence to the contrary, because it was based upon an E3-deleted wt Ad5 (see ¶ linking first and second columns of page 1584). Regarding claim 28, because Ad5 does not comprise a sequence corresponding to positions 311-319 of SEQ ID NO: 12, it is considered that insertion of the gD gene between the packaging signal and E1 gene of Ad-gD-E1A (see, again, Fig. 1) meets this limitation. The viruses were used to induce antibodies to gD in rats, and thus are considered to meet the limitations of claims 31, 32, 34 and 35 (see ¶ linking pages 1585 - 1586). Regarding claim 53, the Ad-gD-E1A virus comprised at least the 400 bp upstream of the "deleted" portion, i.e. upstream from the insertion site of the gD gene, see the explanation above as to why Ad-gD-E1A comprised the first 455 residues of Ad5. Regarding claim 54, the Ad-gD-E1A virus comprised at least the E1 A gene "downstream" of the "deleted" portion, i.e. downstream from

the insertion site of the gD gene. Regarding claim 5, plasmids are disclosed in the legend to Fig. 1, and on pages 1584 to 1585.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MICHAEL BURKHART whose telephone number is (571)272-2915. The examiner can normally be reached on M-F 8AM-5PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michael Burkhart/
Primary Examiner, Art Unit 1633